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Drugs Used to Treat Indigestion in Babies Linked to Higher Rate of Serious Infections

Proton pump inhibitors (PPIs) relieve heartburn in adults, but they're also prescribed to children. A French study reported in JAMA Pediatrics found young children on PPIs had higher rates of bacterial, viral, respiratory and other infections.

By Angelo DePalma, Ph.D.

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A study appearing earlier this month in JAMA Pediatrics reported that children who took proton pump inhibitors (PPIs) for stomach upset experienced a marked increase in infections requiring hospitalization.

PPIs are among the most commonly prescribed drugs in infants and children, and their use is on the rise. They work by attaching to parietal cells in the stomach, where they prevent those cells from releasing hydrochloric acid, which works with enzymes and bile juices to digest food.

A growing body of literature on the acute and long-term side effects of PPIs is causing pediatricians to rethink how these drugs are used, particularly in the very young.

The study group, led by Marion Lassalle, Pharm.D., Ph.D., at the French National Agency for the Safety of Medicines and Health Products, followed more than 1.2 million children born in France between January 2010 and December 2018.

Children were enrolled in the study on receiving their first prescription for any medicine — not just PPIs — to treat digestive issues.

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Children took either PPIs, histamine-2 receptor antagonists, antacids or alginates. Antacids work by combining with and neutralizing stomach acid; alginates coat the stomach to protect it from acid. PPIs and histamine antagonists prevent the release of acid into the stomach.

Children who took PPIs comprised the treatment group, those on other medications were the controls. The study groups were matched for age, sex, access to medical care, size of residence and social deprivation index — a score based on seven social and economic variables.

Children were followed until a hospital admission for serious infection, death or until Dec. 31, 2019, whichever came first.

PPI use was associated with a 34% overall increase in infections requiring hospitalization. Bacterial infections were 56% higher and viral infections increased by 30% in the PPI group.

Infection rates rose by 52% for digestive tract infections, 47% for infections of the ear, nose or throat, 31% for the nervous system, 22% for the lower respiratory tract and 20% for the urinary tract or kidneys.

A much smaller 2019 study also found a connection between PPIs and infections but concluded that adverse events were related to a child's ability to metabolize PPI drugs. Children who were poor metabolizers of PPIs fared worse on those medications than those with normal or elevated levels of a liver enzyme, CYP2C19.

CYP2C19 helps to clear PPIs (and other drugs) from the body. Healthy humans may have high, normal or low levels of this enzyme.

The first U.S.-approved PPI, omeprazol (brand name Prilosec), entered the market in 1989. PPIs quickly replaced histamine-2 receptor antagonists, the leading acid-blocking drugs at the time, based on the former's superior safety, effectiveness and patient acceptance.

Market research firm Coherent Market Insights estimated 2020 global sales of PPIs at $2.9 billion, and predicts annual growth of 4.3% through 2027.

Strengths and weaknesses

According to Lassalle and co-workers, theirs was the first large-scale pediatric investigation into PPIs and pediatric infections.

The strengths of the study were a very large sample size, a capture rate for adverse events approaching 100% and control for socioeconomic factors.

The main weakness was a lack of information on why children received a PPI prescription. Children with the most serious gastrointestinal distress are more likely to have other health issues (including infections), and vice versa, and to receive a PPI prescription.

Sick children also are more likely to experience any drug-related adverse event, including reactions to PPIs. This means that children who are likely to receive a prescription for PPIs are already more likely to experience a serious infection, even if they were not taking a PPI.

The other main limitation was the lack of information on breastfeeding. This factor would normally even out in a 1.2 million-subject study but breastfed babies are less likely to experience serious digestive problems and are better equipped to ward off infections.

They are therefore more likely to take an antacid or alginate than a prescription-only PPI.

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Are PPIs over-prescribed?

In an accompanying editorial Jay Berry, M.D., MPH, and Jonathan Mansbach, M.D., MPH, both of Harvard Medical School, suggest that PPIs are perhaps over-prescribed to otherwise healthy infants.

Gastroesophageal reflux, the medical term for spitting up, is often accompanied by crying, which serves as a signal that the child may be experiencing indigestion.

But babies cry for many different reasons.

PPIs are prescribed to healthy children and to chronically ill children who are more likely to experience digestive issues than healthy babies. Sick children are at additional risk for PPI drug interactions, according to Berry.

"There is no strong evidence to support the use of PPIs in either population," Berry wrote. "Worse: there may be harm."

How do PPIs promote infections?

Lassalle and co-workers posited three possible ways PPIs might promote infections.

Reducing stomach acid alters the gut microbiome, which increases the risk of both viral and bacterial gastrointestinal infections.

The higher incidence of respiratory infections could occur through the gut-lung axis, or from the inhalation of tiny droplets of bacteria-containing fluid from the stomach.

The gut-lung axis is a pathway through which bacteria in the gut control immune responses in the airways.

Disease, dietary changes and drugs, including PPIs, affect populations of these bacteria. A reduction in stomach acid also increases the bacterial content of gastric juices, which increases the likelihood that inhaling them will cause lung infections.

PPI suppression of infection-fighting neutrophils, the most common immune system white blood cell, could account for several other infections, according to the authors.

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PPI side effects

PPIs prevent acid release from cells, but this effect is not limited to the stomach. The drugs also block normal acid production from lysosomes, specialized cells that remove waste products from tissues.

Waste accumulation causes cells and proteins to deteriorate, leading to rapid aging of cells and tissues.

PPI side effects mostly occur after long-term use. A common one, calcium malabsorption, can result in low bone density and fractures. This prompted the U.S. Food and Drug Administration (FDA) in 2011 to issue a warning for over-the-counter PPIs.

The FDA advises individuals at risk for bone fractures to "take adequate vitamin D and calcium supplementation" while on PPIs, not to use the drugs for more than two consecutive weeks, and then no more than three times per year.

Taking PPIs regularly has also been linked to a 44% higher risk for dementia, according to one review — which also concluded that up to 70% of people who take PPIs do not have a condition that warrants taking these drugs.

PPIs also are associated with a 20% to 50% higher incidence of kidney disease and a slightly elevated risk of pneumonia.

Although the FDA has approved most PPIs for children, it notes in an information sheet for pediatric prescribers that the drugs are mostly ineffective in children under age 1. For example, infants treated with one PPI, lansoprazole, for symptoms of crying, fussing or irritability during or after feedings, "showed no difference in the percentage of response than patients treated with a placebo."

PPIs also are associated with tissue- and organ-level changes in the digestive tract, including polyps, thinning of the stomach lining and gastric cancer.

Based on their reading of the Lassalle study, Berry and Mansbach concluded:

> "It is time to limit PPI use in infants and children, especially when they are otherwise healthy and until further investigation distinguishes who has the most favorable risk-benefit ratio.
>
> "To address this knowledge gap, we suggest collecting primary data about the effects of PPI use in infants and children, including changes in the composition and function of [the] infant gut microbiome."

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Angelo DePalma, Ph.D.

Angelo DePalma, Ph.D., is a science reporter/editor for The Defender.

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suzanne romero
7 days ago
either these children are on meds or eating some really unhealthy foods or the mother was when she was pregnant with them no children should be on meds or most adults for that matter i hate big pharma

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SARAB suzanne romero
6 days ago
I think the vaccines really mess up the digestive system.

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BChristine
7 days ago

Indigestion in babies and young children? That's just ***not normal***. There has to be an underlying cause ... I am thinking pesticides, herbicides, glyphosate, other toxins ... maybe passed down via the Mother if we're talking newborns. Or maybe childhood vaccines?

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Wendy ↗ BChristine
7 days ago

Or the most common one, lactose intolerance. Must ask what are you feeding the baby? Mother's milk is the only real baby food until the child gets teeth.

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SHENZI
7 days ago

Are they INSANE??
More and more, when I read things as horrific as this, (and worse) I'm convinced that "THEY" are out to kill as many of us as possible.

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MultiChubby1 ↗ SHENZI
7 days ago

Death by a thousand cuts. Poison you - then give you drugs for the symptoms. This really can't go on much longer.

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Abmeme
7 days ago

Hi, thank you for this info! PPIs also linked/ known to cause C-diff or clostridium difficile.

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SARAB
6 days ago

I can't believe they are giving the PPIs to babies! The medical establishment is SICK.

1 0 Reply • Share ›

unacceptable views
5 days ago

Jesus, this is twisted. I don't take these as an adult because of how dangerous they are. Big Pharma and Big Medicine are laughing all the way to the bank off the backs of weak minded, no EQ parents. The 'why' behind these babies suffering in the first place is the real question.

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